Example 9: Protein Variants

Specification:

The specification describes a protein isolated from liver. A working example shows that the isolated protein was sequenced and determined to have the amino acid sequence shown in SEQ ID NO: 3. The isolated protein was additionally characterized as being 65 kD in molecular weight and having tumor necrosis activity. The specification states that the invention provides variants of SEQ ID NO: 3 having one or more amino acid substitutions, deletions, insertions and/or additions. No further description of the variants is provided. The specification indicates that procedures for making proteins with amino acid substitutions, deletions, insertions and/or additions are routine in the art. The specification does not define when a protein ceases to be a variant of SEQ ID NO: 3.

Claims:

Claim 1. An isolated protein comprising the amino acid sequence shown in SEQ ID NO: 3.

Claim 2. An isolated variant of the protein of claim 1.

Analysis:

Claim 1

Claim 1 is directed to a protein comprising the sequence shown in SEQ ID NO: 3 and the specification describes the complete structure (sequence) of SEQ ID NO: 3. The claimed genus is defined by the presence of this structure. Therefore, one skilled in the art would recognize that the applicant was in possession of a structural feature shared by all members of the genus. The specification does not describe other members of the genus by complete structure. However, given the existing knowledge in the art concerning fusion proteins, which are an example of additions that could be made to SEQ ID NO: 3, those of skill in the art would conclude that the applicant would have been in possession of the claimed genus at the time of filing.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claim 1.

Claim 2

Claim 2 is a genus claim. According to the specification, the term "variant" means a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to SEQ ID NO: 3. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 3.

Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted.

The specification does not describe any members of the claimed genus by complete structure. However, the pre-existing general knowledge in the art supplements the description: additions to the end of known or disclosed proteins resulting in fusion proteins have been described and are generally known. However, the specification does not describe the structure for substitution variants, deletion variants or insertion variants of SEQ ID NO: 3. The specification does not describe the physical or chemical characteristics for substitution variants, deletion variants or insertion variants of SEQ ID NO: 3. The specification does not disclose any correlation(s) between the structure of the variants and SEQ ID NO: 3, or any correlation(s) of structure with variant function.

Although the specification states that these types of amino acid changes are routinely made in the art, the specification and claim do not describe any specific changes to be made. No common structural attributes identify the members of the substitution, deletion and insertion variant genus. Because the disclosure fails to describe the common attributes or characteristics that identify substitution, deletion and insertion variant members of the genus, and because the genus is highly variant, SEQ ID NO: 3 is insufficient to describe the genus, even when considered in light of the general knowledge in the art concerning fusion proteins. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus, and thus, that the applicant was not in possession of the claimed genus. The claimed subject matter is not supported by an adequate written description because a representative number of species has not been described. A rejection under the written description requirement, relying on the analysis set out above, should be entered against the claim to the extent it covers substitution, deletion and insertion variants.

Conclusion:

The specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claim 2.

Example 10: Product Claimed By Its Function

Specification:

The specification discloses a protein isolated from mouse liver that catalyzes the reaction A->B. The isolated protein was sequenced and its sequence was set forth in the specification as SEQ ID NO: 3. The specification also contemplates, but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions are routine in the art and provides an assay for detecting the catalytic activity of the protein or its variants.

Claims:

Claim 1. An isolated protein comprising the amino acid sequence shown in SEQ ID NO: 3.

Claim 2. An isolated variant of a protein comprising the amino acid sequence shown in SEQ ID NO: 3, wherein the variant comprises an amino acid sequence that is at least 95% identical to SEQ ID NO: 3.

Claim 3. The isolated variant of claim 2, wherein the variant catalyzes the reaction A->B.

Analysis:

Claim 1

Claim 1 is directed to a protein comprising the sequence shown in SEQ ID NO: 3. Because it uses open claim language ("comprising"), the claim is generic; *i.e.,* it encompasses proteins that include the sequence of SEQ ID NO: 3 together with other amino acids added to either end of that sequence.

The specification provides an actual reduction to practice of a protein comprising SEQ ID NO: 3 and describes the complete structure (sequence) of SEQ ID NO: 3. The specification describes a method of making a protein comprising SEQ ID NO: 3. The specification describes the function of the described protein (catalyzing the reaction of A->B), although no correlation between this function and the protein's structure is disclosed (e.g., by identifying which amino acids are involved in the active site, substrate binding, etc.). Those skilled in the art would expect that most species within the genus would retain the function of the protein consisting of SEQ ID NO: 3 because each species must include SEQ ID NO: 3 as part of its structure. Thus, predictability of species within the genus is high.

Example 10: Product Claimed By Its Function

The claimed genus of proteins is defined by the presence of the structure represented by SEQ ID NO: 3. Therefore, one skilled in the art would recognize that the applicant was in possession of a structural feature shared by each of the members of the claimed genus at the time of filing. The species shown in the specification's SEQ ID NO: 3 is, therefore, representative of the species within the claimed genus.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to claim 1.

Claim 2

Claim 2 is directed to a variant of the protein defined by claim 1 (a protein comprising SEQ ID NO: 3), where the amino acid sequence of the variant is at least 95% identical to SEQ ID NO: 3. The claim is not limited to variants of the protein of SEQ ID NO: 3 having the function of catalyzing the reaction A->B.

The specification adequately describes proteins comprising the amino acid sequence of SEQ ID NO: 3 (see the analysis of claim 1). All of the proteins within the scope of claim 2 share at least 95% of the amino acid sequence of SEQ ID NO: 3; therefore, the specification describes 95% of the structure that defines the proteins within the claimed genus. All of the species within the genus share a significant degree of partial structure (*i.e.*, at least 95% of SEQ ID NO: 3).

> **Practice Note**
>
> *This example deals only with the written description analysis of the claimed product. Enablement issues that may be raised by the recited facts are not addressed here but should be considered during examination. A separate rejection for nonenablement should be made when appropriate.*

The claimed variants can have amino acid substitutions, deletions, insertions, or additions, as compared to SEQ ID NO: 3. The specification does not provide an actual reduction to practice of any variants of the protein of SEQ ID NO: 3. The specification does not describe the complete structure or physical or chemical properties of any variants of SEQ ID NO: 3, although those skilled in the art would expect members of the genus to have properties similar to those of SEQ ID NO: 3, because of the high degree of structural similarity.

In view of the disclosure of SEQ ID NO: 3, those skilled in the art could readily envision all of the amino acid sequences that are 95% identical to SEQ ID NO: 3. Those skilled in the art could recognize amino acid sequences that are 95% identical to SEQ ID NO: 3 by comparing a given sequence to SEQ ID NO: 3. The presence of an amino acid sequence that is at least 95% identical to SEQ ID NO: 3 is a structural feature of each of the proteins within the claimed genus.

Example 10: Product Claimed By Its Function

The level of skill and knowledge in the art is such that one of ordinary skill would be able to make and identify variants having 95% identity to SEQ ID NO: 3 routinely.

Thus, those skilled in the art would have recognized the disclosure as showing that the applicant was in possession of the claimed genus of protein variants at the time of filing.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to claim 2.

Claim 3

Claim 3 is directed to the genus of variants of SEQ ID NO: 3 that comprise an amino acid sequence at least 95% identical to SEQ ID NO: 3 and catalyze the reaction A->B.

The specification discloses the reduction to practice of one species within the claimed genus; specifically, the protein having the amino acid sequence of SEQ ID NO: 3. There are no drawings or structural formulas disclosed of any other proteins that catalyze the reaction A->B.

The recitation of a polypeptide with at least 95% amino acid sequence identity to SEQ ID NO: 3 represents a partial structure. That is, the claimed proteins share at least 95% of the structure of SEQ ID NO: 3, while 5% of the structure can vary. There is no teaching in the specification regarding which 5% of the structure can be varied while retaining the ability of the protein to catalyze the reaction A->B. Further, there is no art-recognized correlation between any structure (other than SEQ ID NO: 3) and the activity of catalyzing A->B, based on which those of ordinary skill in the art could predict which amino acids can vary from SEQ ID NO: 3 without losing the catalytic activity. Consequently, there is no information about which amino acids can vary from SEQ ID NO: 3 in the claimed genus of proteins and still retain the catalytic activity.

Although the disclosure of SEQ ID NO: 3 combined with the knowledge in the art, would put one in possession of proteins that are at least 95% identical to SEQ ID NO: 3, the level of skill and knowledge in the art is such that one of ordinary skill would not be able to identify without further testing which of those proteins having at least 95% identity to SEQ ID NO: 3 (if any) have the activity of catalyzing the reaction A->B. Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that the applicant was in possession of the claimed genus of proteins based on disclosure of the single species of SEQ ID NO: 3.

Conclusion:

The specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to claim 3.